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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,162	11/29/2006	Tonia Sue Agin	PC25353A	4630

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EXAMINER	
GRASER, JENNIFER E	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
01/19/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~IPGSKala@Pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/578,162	AGIN ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/3/10 has been entered.

Claims 1-20 are currently pending.

Rejections Withdrawn:

The amendment to claim 1 "wherein said live cells are free of neutralizing antibodies or neutralizing antibody fragments" obviates the former 102(b) rejection as anticipated by Thoma et al (US 6,440,408 B2). Support for this new limitation is found in the instant specification at page 3, lines 37-39. Thoma teaches the use of a neutralizing antibody with their live bacterial vaccine. They argue that the prior art has taught that live bacterial vaccines for *in ovo* immunization are unsafe and should not be administered to eggs. They teach that a neutralizing antibody must be used in their vaccines. Accordingly, Thoma teaches away from the instantly claimed invention.

Claim Rejections - 35 USC § 112-Scope of Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods which use live cells of C. jejuni UA535 and C. jejuni 81-176 in the claimed methods, does not reasonably provide enablement for the use of live cells from any species of Campylobacter or any genetically modified Campylobacter strains, or for the use of more than one species of Campylobacter as recited in claim 5. It is noted that 'genetically modified' also encompasses 'attenuated' strains. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to the use of

strains other than C. jejuni UA535 and C. jejuni 81-176, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). With regard to (4) the nature of the invention and (5) the state of the prior art, these are discussed below. The unpredictability (7) was very high as the prior art taught that live *in ovo* vaccination, e.g., wherein the cell is not attenuated or inactivated, of bacterial cells was unsafe and should not be administered to eggs, e.g., Thoma (US 6,440,408). One of skill in the art would require guidance, in order to use the methods as instantly claimed.

The instant invention is drawn to the unexpected discovery that live cells of C.jejuni could be administered in ovo during the final quarter of incubation to induce an immune response in birds against Campylobacter. All of the Examples in the specification teach the administration of either C. jejuni UA535 and C. jejuni 81-176 cells. There are no examples of any other species of Campylobacter or the administration of more than one species at one time. Given the unpredictability of the use of live bacterial cells, it is unclear that any or all species/strains of Campylobacter would have the same unexpected result. The prior art has shown the immunization of live bacterial cells to be harmful. Accordingly, it would take undue experimentation for one of skill in the art to practice the claimed methods with any strain other than C.jejuni. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of

the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention."

Given the lack of guidance contained in the specification, one of skill in the art could not make or use the broadly claimed invention without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-4, 6-8, and 13-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of Ziprin et al (Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999).

Noor et al disclose *in ovo* oral vaccination of chicken eggs with Campylobacter, specifically C.jejuni, which is heat inactivated, at day 16 of

incubation (i.e., final quarter of incubation). See abstract. Noor et al teach that the advantages of in ovo immunization in establishing early immunity are note associated with adverse effects on hatchability or postnatal weight gain. Noor et al teach that in ovo vaccination has been previously reported to induce a higher antibody response in chicks than in postnatal exposure and also resulted in significant improvement in performance. See p. 564, 2nd full paragraph. However, Noor et al do not particularly exemplify the use of live Campylobacter strains in their methods.

Ziprin e al disclose the *in ovo* administration of various live strains of C.jejuni and the effects of mutations in C.jejuni genes on cecal colonization and liver invasion when given in ovo or on day of hatch. Ziprin teach that none of the strains caused morbidity on i.p. challenge though the doses were high. Ziprin teach that by determining the role of the genes studied in colonization, they hope to find some means to prevent C.jejuni from establishing in the gastrointestinal tract of chickens. Several different genetically modified strains were used. Ziprin specifically teach strains with heterologous polynucleotide sequences that encode proteins essential in colonization of domesticated birds by Campylobacter, e.g, *dnaJ* and *cadF* (as outlined on page 3, lines 19-20 of the instant specification). See abstract.

Noor et al teaches the in ovo vaccination of poultry against Campylobacter and Ziprin teaches that the delivery of live, attenuated campylobacter strains in ovo was known in the prior art. It would have been prima facie obvious to one of ordinary skill in the art to substitute a live, especially a live attenuated strain, for

the heat-inactivated strain used in the Noor et al reference because Ziprin teaches that live cells of Campylobacter may be administered in ovo and one of ordinary skill in the art would expect a live, attenuated strain of Campylobacter to provide similar immunogenic results as the heat inactivated strain of Campylobacter. Further, a live attenuated strain would have the ability to be manipulated to produce additional antigens to increase the spectrum of the immune response. A "physiologically acceptable carrier" reads on water and therefore would be inherent in the preparation of the cells for immunization.

5. Claims 5, 16, 17, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of Ziprin et al (Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999), as applied to claims 1-4, 6-8 and 13-15 above and further in view of Ziprin et al (Current Microbiol. 2002. 44: 221-223)..

The teachings of Noor et al and Ziprin et al (Brit. PS) are set forth above. However, they do not specifically teach the additional use of an adjuvant of the use of more than one species in their compositions.

Ziprin et al teach that the prior art has suggested that avirulent viable cell vaccines should be tried for protection against C.jejuni. See first paragraph on page 221. The reference teaches combining several non-colonizing strains of Campylobacter in a 'vaccine cocktail" so that chicks can be exposed to all surface proteins on wild-type colonizing strains. See second paragraph, column 1 on page 221. Ziprin et al teach the use of viable-cell bacterial suspensions and

the use of Ribis's adjuvant. See second column on page 221. The references teaches that 'much previous work has demonstrated that antibody production occurs when embryonated eggs are vaccinated, e.g., *in ovo* vaccination, and cell mediated immune responses 'turn on' about three days after hatch. The instant reference teaches the vaccination of hatched chicks and did not achieve the same results as previous work using *in ovo* administration.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that more than one strain/species of Campylobacter could be used in the method taught by the combination of Noor et al and Ziprin et al (Brit. PS) because Noor et al teach success with the use of a single strain and Ziprin et al (Curr.Microbiol) teaches that combining several non-colonizing strains of Campylobacter in a 'vaccine cocktail" would allow for exposure to all surface proteins on wild-type colonizing strains which would thereby provide for a wider spectrum of coverage against disease factors. Absent evidence to the contrary, the use of multiple species would be expected to raise a more varied immune response. Additionally, the use of an adjuvant in a vaccine composition would have been an obvious addition to enhance the immune response to the vaccine taught by Noor et al and Ziprin et al (Curr.Microbiol) specifically teach the use of Ribis's adjuvant in its Campylobacter vaccines.

6. Claims 9-12 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noor et al (British Poultry Science, 1995. 36(4): 563-573) in view of Ziprin et al (Poultry Science, vol. 78, No. SUPPL 1, 1999, page 39, 88th

Annual Meeting of the Poultry Science Association, Inc., Springsdale, Arkansas, USA,; August 8-11, 1999), as applied to claims 1-4, 6-8 and 13-15 above, in further view of Yokogawa et al (Us 6,410,222 B1).

The teachings of Noor et al and Ziprin et al (Brit. PS) are set forth above. However, they do not specifically teach the additional use of a heterologous antigen from a virus, bacteria or parasite that causes disease in a domesticated bird, or an antigen from an organism that causes food-borne illness in humans, or a protein that can enhance growth or feed efficiency of a domesticated bird.

Yokogawa et al teach the in ovo vaccination of marek's disease type 1 virus. Marek's disease is a chicken infectious disease. Yokogawa et al teach the use of attenuated live viruses into egss in the fourth quarter of incubation. The use of a mixed vaccine is specifically taught from other viruses or bacteria, including Campylobacter spp.. See column 4, lines 36-49. The use of additional antigens are also taught throughout column 4 and the top of column 5 and in the claims.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made that the additional use of a heterologous antigen from a virus, bacteria or parasite that causes disease in a domesticated bird, or an antigen from an organism that causes food-borne illness in humans, or a protein that can enhance growth or feed efficiency of a domesticated bird could be added to the vaccines taught by Noor et al and Ziprin et al (Brit. PS) because multivalent vaccines were well known in the art at the time the invention was made as a means to allow for a broader spectrum of protection against disease

with fewer inoculations. Yokogawa et al is cited to show that, absent evidence to the contrary, the use of an additional antigen would have been an obvious design choice serving to broaden the spectrum of the immune response. Yokogawa et al specifically teaches the use of a mixed vaccine in their live attenuated Marek virus vaccine (for in ovo vaccination) which includes other viruses or bacteria, including Campylobacter spp.. The use of additional antigens against food-borne illness or diseases found in birds would have been obvious choices as heterologous antigens in the vaccines taught by Noor and Ziprin because chickens are consumed by humans and one would want to prevent these types of infections for the safety of the food supply.

Response to Applicants arguments of the 103 rejections of record:

Applicants argue that "Ziprin et al. is directed to colonization experiments, and persistent infection, which is not the same as whether or not any protective immune response has been achieved. "Inducing an immune response" as herein claimed is a specially defined term, provided at page 4, lines 33-37 of the present specification, and there is no demonstration or suggestion in Ziprin et al. that such a protective state has been achieved. Given that the persistently infected bird is harboring an organism that may in fact cause no harm whatsoever-- to the bird-- it is not clear that an immune response would necessarily and reasonably result, and Ziprin et al. does not so state. In effect, when the Examiner declares that Applicant's methods (Page 7 in the Official Action) are the same as the prior art, the result is actually to make a new rejection for inherency, which is not reasonably and predictably supported by the very references on which it is platformed."

These arguments are not commensurate in scope with the claimed invention. A 'protective state' or 'protective immune response' is not required in

the instant claims, e.g., any type of immune response is encompassed regardless of its effectiveness.

Applicants also argue that "Although there are numerous approaches to providing bird flocks which are "Campylobacter-safe" (see Mead at 173) such as pre-colonizing the intestine with other competing bacterial species, there remains the clear problem that avian species are not to be *obviously* expected to mount vigorous immune responses against a microorganism that apparently causes them no harm., and even if an "immune response" is detected, is it of a kind that provides any practical effect and benefit."

These arguments are not commensurate in scope with the claimed invention. A 'vigorous immune response' is not required in the instant claims, e.g., any type of immune response is encompassed regardless of its effectiveness.

Applicants state in their response that "*Ziprin et al* also discloses the in ovo delivery of certain *C. jejuni* strains, and strains containing mutations, to chicken embryos. The subsequent effect on cecal colonization and liver *invasion* in 14-day old in ovo-challenged birds was also measured. No information can be found in this reference that teaches that in ovo delivery" of a live strain of *Campylobacter* induces an immune response which provides some degree of protection against colonization."

These statements have been fully and carefully considered. The in ovo delivery of live strains of Campylobacter by Ziprin et al is the same method which is instantly claimed. The strains set forth in the instant claims include any and/all live strains of any species of Campylobacter, including those which have been genetically modified (which would also include attenuated strains). There is no requirement for any special degree of immune response. Given that the exact

same product is being administered in the same manner, the exact same response would occur. It is noted that the instant specification provides results from the use of C. jejuni UA535 and C. jejuni 81-176 and not *any* Campylobacter species.

Given that Noor teaches a heat-inactivated strain of C.jejuni and Ziprin teaches that the same, non- heat inactivated strain, and that upon high IP challenge did not cause mortality demonstrates that a non-heat activated strain could reasonably be substituted in the method taught by Noor et al. one of ordinary skill in the art would expect a live, attenuated strain of Campylobacter to provide similar immunogenic results as the heat inactivated strain of Campylobacter. Further, a live attenuated strain would have the ability to be manipulated to produce additional antigens to increase the spectrum of the immune response.

Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 8:00 AM-6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

/Jennifer E. Graser/
Primary Examiner, Art Unit 1645

1/13/10